Mitochondria play role in pathogenesis of AD and estrogen-induced neuroprotection

April 6 2008

As the major source of free radicals in cells, mitochondria contribute to the high levels of oxidative stress believed to play a role in the pathogenesis of Alzheimer's disease. Now, a new study from the laboratory of Dr. Roberta Brinton, University of Southern California, demonstrates that estrogen reduces this oxidative stress caused by the mitochondria while increasing the ability of the mitochondria to generate energy – important since there is usually an energy deficit in the Alzheimer brain.

The study was presented April 5 at Experimental Biology 2008 in San Diego by Jia Yao, a graduate student in Dr. Brinton's laboratory. The presentation is part of the scientific program of the American Association of Anatomists (AAA), and Mr. Yao's presentation is a finalist for the AAA Langman Graduate Studet Platform Presentation Award. He also received an AAA travel award.

Mitochondria, small organelles within the cells, use a process called Oxidative Phosphorylation to generate the vast majority of the adenosine triposphate (ATP) molecules that cells utilize to function properly. If the mitochondria become less efficient with age or disease, they use less up oxygen during this process. This inefficiency produces a double hit against the brain: fewer energy molecules being produced and more free radicals being released, leading to damaging oxidative stress.

Using a combination of biochemical and proteomic (protein) approaches, Dr. Brinton's research team demonstrated how estrogen acts

to regulate mitochondrial function in ways pivotal for protection against Alzheimer's disease. These include:

-- an increase of mitochondrial efficiency, enhancing the organelles' ability to generate energy-laden ATP molecules needed by the brain;

-- increased expression of key proteins required for ATP generation;

-- reduction of oxidative stress, protecting neurons from oxidative damage;

-- prevention of excess apoptosis, or programmed cell death, of neurons of the brain;

-- and protection of neurons from mitochondrial toxins, which can induce further mitochondrial dysfunction and cell death.

Source: Federation of American Societies for Experimental Biology